

Refine Search

Search Results -

Terms	Documents
L5 with L6 with (um or umol)	0

Database:

- US Pre-Grant Publication Full-Text Database
- US Patents Full-Text Database
- US OCR Full-Text Database
- EPO Abstracts Database
- JPO Abstracts Database
- Derwent World Patents Index
- IBM Technical Disclosure Bulletins

Search:

L31

Refine Search

Recall Text

Clear

Interrupt

Search History

DATE: Wednesday, January 21, 2004    [Printable Copy](#)    [Create Case](#)

Set Name	Query	Hit Count	Set Name result set
DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ			
L31	l5 with l6 with (um or umol)	0	L31
L30	low calcium same l13	5	L30
L29	l5 and l28	12	L29
L28	permeability with plasmid	83	L28
L27	6086582.pn.	2	L27
L26	kidney and l25	57	L26
L25	gene therapy with permeab\$	121	L25
L24	gene therapy and l23	926	L24
L23	Wolf and permea\$	3708	L23
L22	enhancer with l7	3	L22
L21	l16 with l6 with l18	0	L21
L20	l16 with l13 with l18	0	L20
L19	l18 same l14	98	L19



**Database:**

**Term:**

**Display:**  **Documents in Display Format:**  **Starting with Number**

Search Clear Interrupt

## Search History

**DATE: Wednesday, January 21, 2004**    Printable Copy    Create Case

<u>Set</u> <u>Name</u> side by side	<u>Query</u>	<u>Hit</u> <u>Count</u>	<u>Set</u> <u>Name</u> result set
<i>DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ</i>			
<u>L27</u>	6086582.pn.	2	<u>L27</u>
<u>L26</u>	kidney and l25	57	<u>L26</u>
<u>L25</u>	gene therapy with permeab\$	121	<u>L25</u>
<u>L24</u>	gene therapy and l23	926	<u>L24</u>
<u>L23</u>	Wolf and permea\$	3708	<u>L23</u>
<u>L22</u>	enhancer with l7	3	<u>L22</u>
<u>L21</u>	l16 with l6 with l18	0	<u>L21</u>
<u>L20</u>	l16 with l13 with l18	0	<u>L20</u>
<u>L19</u>	l18 same l14	98	<u>L19</u>
<u>L18</u>	agent or factor	2796548	<u>L18</u>
<u>L17</u>	L16 same l14	0	<u>L17</u>
<u>L16</u>	permea?	1109	<u>L16</u>
<u>L15</u>	l13 with l12	131	<u>L15</u>
<u>L14</u>	L13 same l12	253	<u>L14</u>
<u>L13</u>	gene therapy or gene transfe\$	46591	<u>L13</u>

<u>L12</u>	L10 with l6	2952	<u>L12</u>
<u>L11</u>	L10 same l8	5	<u>L11</u>
<u>L10</u>	serotonin or histamine or VEGF or bradykinin or Platelet-activating factor or IL-2 or zona	50637	<u>L10</u>
<u>L9</u>	L8 with l5	3	<u>L9</u>
<u>L8</u>	l7 with l6	38	<u>L8</u>
<u>L7</u>	permeab\$ agent	617	<u>L7</u>
<u>L6</u>	dna or nucleic or plasmid	223726	<u>L6</u>
<u>L5</u>	calcium ions	22437	<u>L5</u>
<u>L4</u>	poly G with CpG	26	<u>L4</u>
<u>L3</u>	poly G with CpG	26	<u>L3</u>
<u>L2</u>	GGGG motif and CpG	2	<u>L2</u>
<u>L1</u>	CpG motif with GGGG\$	7	<u>L1</u>

END OF SEARCH HISTORY

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L8: Entry 22 of 38

File: USPT

Sep 5, 2000

DOCUMENT-IDENTIFIER: US 6113946 A

TITLE: Self-assembling polynucleotide delivery system comprising dendrimer polycations

Abstract Text (1):

A self-assembling polynucleotide delivery system comprises a dendrimer polycation aiding in the delivery of the polynucleotide to a desired address, and optionally other agents such as DNA masking agents, cell recognition agents, charge-neutralization agents, membrane-permeabilization agents, and subcellular-localization agents.

Brief Summary Text (3):

This invention relates to the field of oligonucleotide delivery systems and gene therapy. In particular, this invention is directed to a self-assembling polynucleotide delivery system comprising a polynucleotide and a dendrimer polycation, and optionally other agents, aiding the delivery of the polynucleotide to a desired subcellular-location. The polynucleotide and the other agents are in general associated with the polynucleotide via non-covalent interactions. Agents suitable for use herein include DNA-masking components, cell recognition agents, charge-neutralization agents, membrane-permeabilization agents, and subcellular localization agents, among others.

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L28: Entry 22 of 83

File: USPT

Feb 4, 2003

DOCUMENT-IDENTIFIER: US 6514947 B2

TITLE: Formulated nucleic acid compositions and methods of administering the same for gene therapy

Detailed Description Text (85):

While not being limited in scope by any theory set forth, several mechanisms of action of amphiphilic polymers may account for the observed results including: Stabilization of plasmid DNA complexes due to coating; increased cell membrane permeability, thereby allowing easier passage of the plasmid DNA complex through the cell; membrane and/or volume exclusion, increasing the concentration of plasmid DNA complexes at the cell surface. Poloxamer 407.RTM. has been shown to improve the transduction efficiency of adenoviral vectors by apparently maintaining a high pericellular concentration of the vector or by disrupting the cell membrane. K. March et al. Facilitation of Adenoviral Gene Delivery by Poloxamer 407.RTM.. Proceed. Intern. Symp. Control. Rel. Bioact. Mater., 21 (1994).

First Hit

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L19: Entry 10 of 98

File: PGPB

Oct 16, 2003

DOCUMENT-IDENTIFIER: US 20030195495 A1

TITLE: Transvascular TMR device and method

Detail Description Paragraph:

[0063] Various therapeutic agents may be infused into the channels through the infusion catheter. Growth factors, genetic therapeutic agents and other means for gene therapy may be injected into the newly created TMR channels while the channeling catheter is still in the channel. Of particular utility is the vascular endothelial growth factor (VEGF) which may be injected directly into the TMR channels to encourage endothelial cells to proliferate and form new capillaries, and may encourage the myocardial cells lining the channel to differentiate into endothelial cells. Several substances such as phVEGF165 (DNA that encodes for VEGF), many mitogens including endothelial cell specific mitogens, growth factors similar to VEGF, vascular permeability factor, basic or acidic fibroblast growth factor may be infused. Rather than inject the growth factor itself, DNA encoded for vascular endothelial growth factor can be perfused. Human 293 cells may be infused to promote proliferation of endothelial cells. Each of these compounds is known to produce beneficial effects.

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L28: Entry 31 of 83

File: USPT

Jul 24, 2001

DOCUMENT-IDENTIFIER: US 6265387 B1

TITLE: Process of delivering naked DNA into a hepatocyte via bile duct

## CLAIMS:

1. A method for delivering naked plasmid DNA into a hepatocyte of a mammal comprising:

a) injecting a composition into the bile duct of a mammal, said composition consisting of naked plasmid DNA encoding a protein operably linked to a promoter and a pharmacologically acceptable solution; and

b) increasing the permeability of said bile duct to allow the composition through the bile duct wall and into the liver of the mammal such that said plasmid DNA is delivered to a hepatocyte of the liver, and said hepatocyte expresses said protein to a detectable level.



[First Hit](#)   [Fwd Refs](#)**End of Result Set**☐ **Generate Collection** **Print**

L9: Entry 3 of 3

File: USPT

Apr 23, 2002

US-PAT-NO: 6376471

DOCUMENT-IDENTIFIER: US 6376471 B1

TITLE: Gene delivery compositions and methods

DATE-ISSUED: April 23, 2002

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Lawrence, III; John H.	Reisterstown	MD		
Donahue; J. Kevin	Baltimore	MD		

US-CL-CURRENT: 514/44; 424/93.2, 435/320.1, 435/455

## CLAIMS:

What is claimed is:

1. A method for delivering nucleic acid to cells in tissue of interest, comprising:

administering to the cells a permeability agent to increase vascular permeability of the cells to an exogenous nucleic acid;

administering the exogenous nucleic acid to the cells under an effective amount of low calcium ion concentrations of about 500 .mu.mol/L or less; whereby the delivery of the nucleic acid to the cells is enhanced.

2. The method of claim 1 wherein the nucleic acid is administered to the cells under calcium ion concentrations of about 40 .mu.mol/L to about 500 .mu.mol/L.

3. The method of claim 1 wherein the nucleic acid is administered by perfusion.

4. The method of claim 3 wherein a perfusate of nucleic acid is recirculated and then readministered to the cells.

5. The method of claim 1 wherein the permeability agent is serotonin, bradykinin, platelet-activating factor, prostaglandin E.sub.1, histamine, vascular endothelium growth factor, zona occludens toxin, interleukin-2, plasma kinins, L-N-monomethyl arginine or L-N-nitro-arginine methyl ester.

6. The method of claim 1 wherein the permeability agent exhibits at least about 5% of the permeability activity of bradykinin in a standard permeability assay.

7. The method of claim 1 wherein the permeability agent is perfused through vasculature of the tissue prior to administration of the nucleic acid.
8. The method of claim 1 wherein said low calcium ion concentrations are provided by perfusing through vasculature of the tissue a fluid having a calcium ion concentration of from about 40  $\mu\text{mol/L}$  to about 500  $\mu\text{mol/L}$ .
9. The method of claim 1 wherein the nucleic acid is administered to a solid cell mass.
10. The method of claim 1 wherein the nucleic acid is administered to a solid organ.
11. The method of claim 1 wherein the nucleic acid is administered to the cells of heart, lung, kidney, testes, ovaries, skeletal muscle, kidneys, brain or spleen.
12. The method of claim 1 wherein the tissue is cardiac tissue.
13. The method of claim 1 wherein the tissue is liver tissue.
14. The method of claim 1 wherein the tissue comprises malignant cells.
15. The method of claim 1 wherein the nucleic acid is administered to a solid tumor.
16. The method of claim 1 wherein the tissue is mammalian.
17. The method of claim 1 wherein the nucleic acid is administered ex vivo.
18. The method of claim 1 wherein the nucleic acid is administered in vivo.
19. The method of claim 1 wherein the nucleic acid is administered to a human.
20. The method of claim 1 wherein the nucleic acid is administered to livestock, poultry or dog or cat.
21. A method for delivering nucleic acid to malignant cells in targeted tissue, comprising:  
  
administering to the cells a permeability agent to increase vascular permeability of the cells to an exogenous nucleic acid;  
  
administering the exogenous nucleic acid to the cells under an effective amount of low calcium ion concentrations of about 500  $\mu\text{mol/L}$  or less; whereby the delivery of the nucleic acid to the cells is enhanced.
22. The method of claim 21 wherein the nucleic acid is administered to the cells under calcium ion concentrations of about 40  $\mu\text{mol/L}$  to about 500  $\mu\text{mol/L}$ .
23. The method of claim 21 wherein the nucleic acid is administered by perfusion.
24. The method of claim 23 wherein a perfusate of nucleic acid is recirculated and then

readministered to the cells.

25. The method of claim 21 wherein the permeability agent is serotonin, bradykinin, platelet-activating factor, prostaglandin E.sub.1, histamine, vascular endothelium growth factor, zona occludens toxin, interleukin-2, plasma kinins, L-N-monomethyl arginine or L-N-nitro-arginine methyl ester.

26. The method of claim 21 wherein the permeability agent exhibits at least about 5% of the permeability activity of bradykinin in a standard permeability assay.

27. The method of claim 21 wherein the permeability agent is perfused through vasculature of the tissue prior to administration of the nucleic acid.

28. The method of claim 21 wherein a fluid is perfused through vasculature of the tissue by a fluid having a calcium ion concentration of from about 40 .mu.mol/L to about 500 .mu.mol/L.

29. The method of claim 21 wherein said targeted tissue comprises a solid tumor comprising the malignant cells.

30. The method of claim 21 wherein the malignant cells are present in a lung, liver, prostate, brain, testes or ovaries of a subject.

31. The method of claim 21 wherein the nucleic acid is administered to a human.

32. A method for delivering nucleic acid to cells in tissue of interest, comprising:

administering to the cells i) a permeability agent to increase vascular permeability of the cells to an exogenous nucleic acid, and ii) the exogenous nucleic acid under an effective amount of low calcium ion concentrations of about 500 .mu.mol/L or less, whereby the delivery of the nucleic acid to the cells is enhanced.

33. The method of claim 32 wherein the nucleic acid is administered to the cells under calcium ion concentrations of about 40 .mu.mol/L to about 500 .mu.mol/L.

34. The method of claim 32 wherein the nucleic acid is administered by perfusion.

35. The method of claim 34 wherein the perfusate of nucleic acid is recirculated and then readministered to the cells.

36. The method of claim 32 wherein the permeability agent is serotonin, bradykinin, platelet-activating factor, prostaglandin E.sub.1, histamine, vascular endothelium growth factor, zona occludens toxin, interleukin-2, plasma kinins, L-N-monomethyl arginine or L-N-nitro-arginine methyl ester.

37. The method of claim 32 wherein the permeability agent exhibits at least about 5% of the permeability activity of bradykinin in a standard permeability assay.

38. The method of claim 32 wherein the permeability agent is perfused through vasculature of the tissue prior to administration of the nucleic acid.

39. The method of claim 32 wherein low calcium ion concentration conditions are provided by perfusing through vasculature of the tissue a fluid having a calcium ion concentration of from about 40  $\mu\text{mol/L}$  to about 500  $\mu\text{mol/L}$ .

40. A nucleic acid enhanced delivery kit comprising:

a permeability agent that increases vascular permeability of a subject; a nucleic acid for administration to a subject; and a solution having an effective amount of a calcium ion concentration that enhances the delivery of the nucleic acid to the subject, wherein said concentration is about 500  $\mu\text{mol/L}$  or less.

41. The kit of claim 40 further comprising a device for delivery of the nucleic acid.

42. The kit of claim 40 wherein the delivery device is a catheter.

43. The kit of claim 40 wherein the nucleic acid is present in the kit as a viral vector.

44. The kit of claim 40 wherein the solution has a calcium ion concentration of about 40  $\mu\text{mol/L}$  to about 500  $\mu\text{mol/L}$ .

45. A treatment solution comprising:

a permeability agent that increases vascular permeability of cells to an exogenous nucleic acid; a nucleic acid; and a solution having an effective amount of a calcium ion concentration that enhances the delivery of the nucleic acid to the cells, wherein said concentration is about 500  $\mu\text{mol/L}$  or less.

46. The solution of claim 45 wherein the solution is pharmaceutically acceptable.

47. The solution of claim 45 wherein the solution comprises one or more therapeutic agents in addition to the nucleic acid.

48. The solution of claim 45 wherein the solution comprises one or more vascular permeability agents.

49. The solution of claim 45 wherein the permeability agent is serotonin, bradykinin, platelet-activating factor, prostaglandin E<sub>1</sub>, histamine, vascular endothelium growth factor, zona occludens toxin, interleukin-2, plasma kinins, L-N-monomethyl arginine or L-N-nitro-arginine methyl ester.

50. The solution of claim 45 wherein the solution has a calcium ion concentration of about 40  $\mu\text{mol/L}$  to about 500  $\mu\text{mol/L}$ .

(FILE 'MEDLINE, CANCERLIT, EMBASE, BIOSIS, BIOTECHDS, CAPLUS' ENTERED AT  
17:03:04 ON 21 JAN 2004)

DEL HIS

L1	1690484	S	CALCIUM
L2	472879	S	PERMEAB?
L3	52142	S	L2 AND L1
L4	3574007	S	DNA OR NUCLEIC OR PLASMID
L5	1607	S	L4 AND L3
L6	29520	S	UM
L7	1	S	L6 AND L5
L8	3227	S	UMOL?
L9	0	S	L8 AND L5
L10	9700	S	LOW CALCIUM
L11	260	S	L10 AND L2
L12	13	S	L11 AND L4
L13	7	DUP REM	L12 (6 DUPLICATES REMOVED)
L14	163	S	L5 AND IONS
L15	231266	S	GENE THERAPY OR GENE TRANSFE? OR NUCLEIC ACID TRANSFE? OR NUC
L16	6	S	L15 AND L14
L17	6	DUP REM	L16 (0 DUPLICATES REMOVED)
L18	36	S	CALCIUM IONS AND (UM OR UMOL)
L19	6	S	L18 AND L4
L20	6	DUP REM	L19 (0 DUPLICATES REMOVED)

L13 ANSWER 2 OF 7 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
AN 1999-08808 BIOTECHDS  
TI Increasing delivery of **nucleic** acid to tissues by increasing  
vascular **permeability**;  
such as antisense oligonucleotide and ribozyme and transgenic animal  
used for tumor therapy, gene therapy and in xenotransplantation  
AU Lawrence J H; Donahue K J  
PA Univ.Johns-Hopkins  
LO Baltimore, MD, USA.  
PI WO 9918792 22 Apr 1999  
AI WO 1998-US21354 8 Oct 1998  
PRAI US 1997-62018 10 Oct 1997  
DT Patent  
LA English  
OS WPI: 1999-277358 [23]  
AB A method for improving transfer of **nucleic** acids to a target  
tissue by increasing vascular **permeability** is new and involves  
treating the tissue with an agent that increases vascularity. The  
**nucleic** acid is particularly included in a virus vector. Also  
claimed are a pharmaceutical kit containing the **nucleic** acid  
and the agent and a treatment solution containing the **nucleic**  
acid in a liquid carrier of **low calcium** ion  
concentration. The method can be used to deliver **nucleic** acids  
for expression of therapeutically active gene products in target tissues,  
in human or veterinary medicine, particularly for treatment of solid  
tumors or in xenogenic cells (e.g. pig or primate) intended for  
transplantation. The therapeutic application could be the delivery of  
vasoactive, angiogenic, antirhythmic, anticancer and anti-angiogenic  
agents, including antisense sequences and ribozymes that inhibit  
expression of a diagnostic agent, e.g. a marker protein, or is used to  
study the effect of a heterologous gene on an intact animal, to create  
animal models of disease or to study disease processes. (32pp)

L13 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 2002:293485 CAPLUS  
 DN 136:304118  
 TI Methods and compositions for **nucleic** acid delivery  
 IN Donahue, Kevin J.; Marban, Eduardo; Nagata, Koichi; Lawrence, John H.  
 PA Johns Hopkins University, USA  
 SO PCT Int. Appl., 91 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002030470	A1	20020418	WO 2001-US32274	20011015
	WO 2002030470	C2	20030206		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	AU 2002014596	A5	20020422	AU 2002-14596	20011015
	US 2002094326	A1	20020718	US 2001-977865	20011015
	EP 1331950	A1	20030806	EP 2001-983146	20011015
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			

PRAI US 2000-240231P P 20001013  
 WO 2001-US32274 W 20011015

AB The present provides methods and compns. that enable effective delivery of **nucleic** to desired cells, including to a solid organ such as a mammalian heart. The methods and compns. enable effective gene transfer and subsequent expression to a majority of cells throughout a solid organ such as the heart. Methods and compns. of the invention preferably provide enhanced vascular **permeability** that enables increased gene transfer to targeted cells, but without significant degrdn. or injury to endothelial cell layers. It has been shown that administration of one or more phosphodiesterase (PDE) inhibitors, particularly a PDE-5 inhibitor such as sildenafil can enhance **nucleic** acid delivery to a solid cell mass by amplifying endogenous cGMP and thereby causing an increase in vascular **permeability**. It was shown that particularly enhanced **nucleic** acid delivery resulted from combined administration of a PDE-5 inhibitor and another **permeability** enhancement agent such as VEGF. It has been shown that.